## WORKSHEET for Evidence-Based Review of Science for Emergency Cardiac Care

### Worksheet author(s)

| Valeria Rac, Dirk Mueller | Date Submitted for review: March 6, 2009 |

### Clinical question.

In patients with STEMI in the prehospital setting (P), does the use of prehospital fibrinolytics (I), compared with inhospital fibrinolytics (C), improve outcome (eg. chest pain resolution, infarct size, ekg resolution, survival to discharge, 30/60 d mortality) (O)?

### Is this question addressing an intervention/therapy, prognosis or diagnosis?

Intervention

### State if this is a proposed new topic or revision of existing worksheet

Partial revision with added outcome.

### Conflict of interest specific to this question

Do any of the authors listed above have conflict of interest disclosures relevant to this worksheet? No.

### Search strategy (including electronic databases searched).

PubMed (1948 to 2009) "ST elevation myocardial infarction" (all fields) and MeSH (heading) then prehospital fibrinolytics" (all fields) and MeSH (heading) then combined search results. Also searched “Acute Myocardial Infarction” (all fields) and MeSH (heading) then "Fibrinolytics" (all fields) and MeSH (heading) and then "EMS" "prehospital" (all fields) then combines the search results.

EMBASE search (1980 to 2009 and EMBASE Classic 1947-1979) using text words (all fields) prehospital fibrinolytics and ST elevation myocardial infarction.

AHA EndNote Master Library, Cochrane database for systematic reviews, Central Registry of Controlled Trials, Review of references from articles, Related links and Google scholar.

### State inclusion and exclusion criteria

The following studies were excluded: studies that compare use of prehospital fibrinolytics with primary angioplasty/PCI (not inhospital, fibrinolysis) (11), study with fibrinolytics done in inhospital setting (1), studies looking into combined effect of prehospital fibrinolysis and other drugs without inhospital lysis group (2), and study reporting a feasibility of 12 lead in prehospital setting (1).

### Number of articles/sources meeting criteria for further review:

32 studies met criteria for further review. Of these 14 studies were LOE 1, 10 studies were LOE 2, three studies were LOE 3, and five studies were LOE 4.
# Summary of evidence

## Evidence Supporting Clinical Question

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<thead>
<tr>
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<tr>
<td>Rawles, GREAT 2003 F</td>
<td>Welsh, 2006 F</td>
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A = Chest pain resolution  
B = Infarct size (reduction)  
C = EKG resolution  
D = Survival to discharge/hospital mortality  
E = 30/60 d mortality  
F = Other endpoints  

* denotes key article(s)
### Evidence Neutral to Clinical question

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#### Level of evidence

- A = Chest pain resolution
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![denotes key article(s)]

### Evidence Opposing Clinical Question

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- A = Chest pain resolution
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Evidences from different studies are quite promising demonstrating that fibrinolysis administered in prehospital setting is safe and feasible treatment strategy for STEMI patients. Furthermore most studies have shown significant reduction in time to treatment which consequently improved patients’ outcome such as chest pain (Weaver, 1995; Rozenman, 1995) and EKG resolution (Trent, 1994; Weiss, 1998), infarct size reduction, decreased mortality (GREAT, 1992; EMIP, 1993; Rawles, 1994; Rawles, 1996; Rawles 1997; Morrison, 2000; Mathew, 2003).

Meta-analysis done by Morrison, 2000 that pooled six RCT studies (n=6434 and three follow-up studies suggested that prehospital fibrinolysis significantly decreased the time to thrombolysis intervals (prehospital group 104 (7) minutes and inhosptal group 162 (16) minutes; time difference was approximately 60 minutes (p=0.007) and all-cause hospital mortality (odds ratio 0.83; 95% confidence interval 0.70-0.98; z score=-2.14; p=0.03).

In 1992 GREAT study group (n=311; prehospital group n=163 got anistreplase 30 units i.v. at home; inhospital group n=148 got the same treatment in hospital) has also shown reduction in the onset of symptom to time to treatment interval (prehospital group 101 minutes and inhosptal group 240 minutes (median times)). Adverse events were not more common in prehospital setting and fewer deaths from all causes were reported in prehospital group within three months with relative reduction of 49% (prehospital group 13/163 (8%); inhospital group 23/148 (15.5%); difference -7.6% with 95% confidence interval -14.7% to -0.4%; p=0.04). GREAT study has pointed out that prehospital group who received treatment at home had better left ventricular function and less common full thickness Q wave infarction (65/122 (53.3%) v 76/112 (67.9%); difference -14.6% with 95% confidence interval -27.0% to -2.2%; p=0.02). Beneficial effect of prehospital fibrinolysis was the most prominent when the treatment was administered within two hours of symptom onset.

Prehospital fibrinolysis was associated with EKG/ECG evidence of increased myocardial reperfusion and reported as a reduction of >25% in the single lead demonstrating greatest ST elevation on the presenting EKG/ECG (prehospital group 37/63 (59%); inhospital group 23/68 (34%); difference 25% with 95% confidence interval 8% to 42%; p=0.003) (Trent, 1994).

One year mortality was 17/163 patients (10.4%) in prehospital group compared with 32/148 (21.6%) in inhospital group (relative reduction 52%, with 95% confidence interval 14% to 89%; p = 0.007) (Rawles, 1994). Interestingly in patients presenting two hours after symptoms onset each hour's delay in receiving the treatment led to the loss of 21/1000 lives within 30 days (95% confidence interval 1 to 94/1000 lives; p=0.03) and 69/1000 lives within 30 months (16 to 141/1000 lives; p=0.0004) (Rawles, 1996).

5 year mortality in prehospital group was 41/163 (25%) compared with 53/148 (36%) in the hospital treatment group (log-rank test, p<0.025). Furthermore 1 h delay in the lysis treatment was associated with an increased death hazard ratio by 20%, equivalent to the loss of 43/1000 lives within the next 5 years (95% confidence interval 7 to 88; p=0.012). 30 min treatment delay reduces the average expectation of life by approximately 1 year (Rawles, 1997).

10 year mortality in the prehospital group was 73/163 (44.78%), and 69/148 (46.62%) in the hospital group with no statistical difference between the two groups. The area between the survival curves of two groups is equivalent to 0.9 (95% confidence interval -0.1 to 1.9; 7.4 v 6.5) years, and this represents the additional survival benefit enjoyed on average by each of the patients treated in prehospital setting in comparison those in the hospital group during 10 years follow up (Rawles, 2003).

In a study done by Weaver, 1993 patients (n=360) received aspirin and alteplase either in prehospital setting (n=175) or in hospital (n=185). Study has reported decreased interval from symptom onset to treatment in prehospital group from 110 to 77 minutes (P < .001). More patients in prehospital group had resolution of pain by admission (23% vs 7%; P < .001). However there were no significant differences in the composite score (death, stroke, serious bleeding and infarct size) (P = .64), mortality (5.7% vs 8.1%), ejection fraction (53% vs 54%), or infarct size (6.1% vs 6.5%). Interestingly a secondary analysis of time to treatment and outcome demonstrated that treatment initiated within 70 minutes of symptom onset was associated with better outcome (composite score, P = .009; mortality, 1.2% vs 8.7%, P = .04; infarct size, 4.9% vs 11.2%, P < .001; and ejection fraction, 53% vs 49%, P = .03) than later initiated treatment. In this study identification of eligible patients, 12 lead ECG acquisition and administration of fibrinolytic were done by paramedics; ED physicians in 6 base hospitals reviewed the findings over the phone and finalized decision to randomize a patient. In the same study population follow-up study done by Brouwer, 1996 has shown that long-term survival and survival free of death or readmission to the hospital for angina, myocardial infarction, congestive heart failure, or revascularization did not differ significantly between the groups. For prehospital group two-year survival was 89% and for inhospital group 91% (p = 0.46). Furthermore event-free survival at 2 years in prehospital group was 56% compared to and 64% in inhospital group (p = 0.42).

EMIP group (1993) studied the efficacy of fibrinolytic therapy in a multicenter, randomized double-blind study where 2750 patients received anistreplase before admission, followed by placebo in the hospital (prehospital group), and 2719 received placebo before admission, followed by anistreplase in the hospital (hospital group). The patients in the prehospital group received treatment 55 minutes earlier than those in the hospital group. However there was a nonsignificant reduction in overall mortality at 30 days in the prehospital group (9.7 percent vs. 11.1 percent in the hospital group; reduction in risk, 13 percent; 95 percent confidence interval, -1 to 26 percent; P = 0.08). Prehospital group had significantly less death from cardiac causes compared to inhospital group (8.3
percent vs. 9.8 percent; reduction in risk, 16 percent; 95 percent confidence interval, 0 to 29 percent; \( P = 0.049 \). However adverse events occurred more frequently in the prehospital group during the period preceding hospitalization such as ventricular fibrillation (\( P = 0.02 \)), shock (\( P < 0.001 \)), symptomatic hypotension (\( P < 0.001 \)), and symptomatic bradycardia (\( P = 0.001 \)).

Welsh, 2006 conducted a prospective observational comparative cohort of all patients with STEMI during ASSENT 3+ study enrollment (North American paramedic setting, Canada). During the 22-month study period complete STEMI cohort had 1095 patients; 119 patients received fibrinolysis in prehospital setting; 673 patients received inhospital fibrinolysis, 170 received primary PCI and 133 patients received no reperfusion. Paramedics were responsible for recognition of STEMI patients, preliminary ECG interpretation and prehospital patient clinical assessment. They received support from study physicians. Time-to-treatment interval was reduced in prehospital group compared to inhospital group (1 hour 43 minutes vs 2 hours 38 minutes; \( P < .001 \)). Furthermore prehospital patients displayed more favorable outcomes: peak creatine kinase (1413 vs 1549 U/L; \( P = .122 \)), Q wave at discharge (56.3% vs 70.7%; \( P = .003 \)), and intracranial hemorrhage (0% vs 0.8%; \( P < 1.0 \)). However there was no significant difference in inhospital mortality for prehospital versus inhospital group (3.4% versus 4.8% (\( P = .627 \)), with an adjusted odds ratio of 0.60 and confidence interval, 0.19-1.87).

**Acknowledgements:** NIL

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**Citation List**

[1-32]

   

   

   

   

   
   Level 1. Fair. Supportive/neutral.

   
   Level 2. Good. Supportive/neutral.

   
   Level 2. Fair. Supportive.

Level 1. Fair. Supportive.


Level 1. Good. Supportive.


Level 3. Fair. Supportive.


Level 1. Good. Supportive.


Level 2. Good. Supportive/neutral.


Level 1. Good. Supportive/opposing for different outcome measures.


Level 1. Good. Supportive.


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   Level 2. Fair. Supportive/opposing.


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